

CLAIMS

1. A calcium channel  $\alpha_2\delta$  subunit that is soluble and retain the functional characteristics of the full-length or wild-type  $\alpha_2\delta$  subunit from which it derives.
- 5 2. A calcium channel  $\alpha_2\delta$  subunit according to claim 1 wherein the full-length or wild-type  $\alpha_2\delta$  subunit from which it derives is of mammalian origin.
3. A calcium channel  $\alpha_2\delta$  subunit according to claim 2 wherein the mammalian origin is a human, a porcine, a rat or a mouse origin.
4. A calcium channel  $\alpha_2\delta$  subunit according to claim 3 wherein the mammalian origin is  
10 a human origin.
5. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 4, wherein the full-length or wild-type  $\alpha_2\delta$  subunit from which it derives is naturally expressed in the cerebral cortical.
6. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 5, wherein the  
15 full-length or wild-type  $\alpha_2\delta$  subunit from which it derives is voltage-dependent.
7. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 6, wherein the  $\alpha_2\delta$  subunit is cleaved.
8. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 7, wherein the  $\alpha_2\delta$  subunit is cleaved into separate  $\alpha_2$  and  $\delta$  peptides.
- 20 9. A calcium channel  $\alpha_2\delta$  subunit according to claim 8, wherein the  $\alpha_2$  and  $\delta$  peptides are disulfide-bridged.
10. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 6, wherein the  $\alpha_2\delta$  subunit is not cleaved.
11. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 10 characterized  
25 in that it is purified or isolated.
12. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 11 characterized in that it is processed as the full-length or wild-type  $\alpha_2\delta$  subunit from which it derives is naturally processed.
13. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 12 characterized  
30 in that it is producable by the baculovirus/insect cells expression system.
14. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 13 characterized in that it is produced by the baculovirus/insect cells expression system.
15. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 14 characterized in that its  $\delta$  peptide comprises at least the ligand-interacting part(s) of the complete  $\delta$   
35 peptide from which it originates
16. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 15 characterized in that its  $\delta$  peptide has a C-terminal truncation with respect to the complete  $\delta$  peptide

from which it originates, said truncation being sufficient to render the truncated  $\delta$  peptide soluble.

17. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 16 characterized in that its  $\alpha_2$  peptide comprises at least the ligand-interacting part(s) of the complete  $\alpha_2$  peptide from which it originates.
18. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 15 or 17 characterized in that ligand is gabapentin, L-Norleucine, L-Allo-Isoleucine, L-Methionine, L-Leucine, L-Isoleucine, L-Valine, Spermine or L-Phenylalanine.
19. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 18 characterized in that its  $\alpha_2$  peptide comprises at least the ligand-interacting part(s) of the complete  $\alpha_2$  peptide from which it originates, its  $\delta$  peptide comprises at least the ligand-interacting part(s) of the complete  $\delta$  peptide from which it originates and its  $\delta$  peptide does not comprise a part of the transmembrane domain of the complete  $\delta$  peptide from which it originates which renders said calcium channel insoluble.
20. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 19 wherein the full-length or wild-type  $\alpha_2\delta$  subunit from which it derives or originates is  $\alpha_2\delta$ -2,  $\alpha_2\delta$ -3 or  $\alpha_2\delta$ -4.
21. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 20 wherein the full-length or wild-type  $\alpha_2\delta$  subunit from which it derives or originates has the amino acid sequence of SEQ ID N°20.
22. A calcium channel  $\alpha_2\delta$  subunit according to claim 20 or 21 characterized in that the amino acid sequence of its unprocessed form comprises or consists of SEQ ID N° 4, SEQ ID N° 5 or SEQ ID N° 6.
23. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 20 to 22 characterized in that the amino acid sequence of its unprocessed form comprises or consists of the region comprised between amino acid number 340 and amino acid number 1062 of SEQ ID N°20.
24. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 20 wherein the full-length or wild-type  $\alpha_2\delta$  subunit from which it derives or originates has the amino acid sequence of SEQ ID N°21.
25. A calcium channel  $\alpha_2\delta$  subunit according to claim 20 or 24 characterized in that the amino acid sequence of its unprocessed form comprises or consists of SEQ ID N° 10, SEQ ID N° 11 or SEQ ID N° 12.
26. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 20, 24 or 25 characterized in that the amino acid sequence of its unprocessed form comprises or consists of the region comprised between amino acid number 306 and amino acid number 1019 of SEQ ID N°20.

27. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 20 wherein the full-length or wild-type  $\alpha_2\delta$  subunit from which it derives or originates has the amino acid sequence of SEQ ID N°55.
28. A calcium channel  $\alpha_2\delta$  subunit according to claim 20 or 27 characterized in that the amino acid sequence of its unprocessed form comprises or consists of SEQ ID N° 53, SEQ ID N° 54 or SEQ ID N° 55.
29. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 20, 27 or 28 characterized in that the amino acid sequence of its unprocessed form comprises or consists of the region comprised between amino acid number 302 and amino acid number 1050 of SEQ ID N°55.
30. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 20 wherein the full-length or wild-type  $\alpha_2\delta$  subunit from which it derives or originates has the amino acid sequence of SEQ ID N°33 or SEQ ID N°44.
31. A calcium channel  $\alpha_2\delta$  subunit according to claim 20 or 30 characterized in that the amino acid sequence of its unprocessed form comprises or consists of SEQ ID N° 34, SEQ ID N° 35, SEQ ID N° 36, SEQ ID N° 41, SEQ ID N° 42 or SEQ ID N° 43.
32. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 20, 30 or 31 characterized in that the amino acid sequence of its unprocessed form comprises or consists of the region comprised between amino acid number 302 and amino acid number 1018 of SEQ ID N°33 or SEQ ID N°44.
33. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 20, 30 or 31 characterized in that the amino acid sequence of its unprocessed form comprises or consists of the region comprised between amino acid number 302 and amino acid number 1018 of SEQ ID N°33 or SEQ ID N°44.
34. A calcium channel  $\alpha_2\delta$  subunit according to any one of claims 20, 30, 31, 32 or 33 characterized in that its  $\alpha_2$  peptide comprises the region comprised between amino acid number 302 and amino acid number 946 or 997 of SEQ ID N°33 or of SEQ ID N°44 and its  $\delta$  peptide comprises the region comprised between amino acid number 984 and amino acid number 1018 of SEQ ID N°33 or of SEQ ID N°44.
35. A calcium channel  $\alpha_2\delta$  subunit characterized in that its  $\alpha_2$  peptide and its  $\delta$  peptide have 99%, 98%, 97%, 96%, or 95% homology or identity with the  $\alpha_2$  peptide and the  $\delta$  peptide respectively of a calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 34.
36. A nucleic acid molecule characterized in that its nucleotide sequence comprises a nucleotide sequence which encodes a calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 35.

37. A nucleic acid molecule characterized in that its nucleotide sequence comprises a nucleotide sequence which encodes the  $\alpha_2$  peptide or the  $\delta$  peptide of a calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 35.
38. A nucleic acid molecule which hybridizes under stringent conditions with a nucleic acid molecule according to claim 36, 37 or 39.
39. A nucleic acid molecule according to any one of claims 36 to 38 which comprises SEQ ID N°1, SEQ ID N°2, SEQ ID N°3, SEQ ID N°7, SEQ ID N°8, SEQ ID N°9, SEQ ID N°13, SEQ ID N°14, SEQ ID N°15, SEQ ID N°30, SEQ ID N°31, SEQ ID N°32, SEQ ID N°38, SEQ ID N°39, SEQ ID N°40, SEQ ID N°50, SEQ ID N°51, or SEQ ID N°52.
40. A vector capable of expressing a nucleic acid molecule according to any one of claims 36 to 39.
41. An expression vector comprising a nucleic acid molecule according to any one of claims 36 to 39.
42. A vector according to claim 40 or 41 which is a baculovirus vector.
43. A cell comprising a nucleic acid molecule according to any one of claims 36 to 39.
44. A cell comprising a vector according to claim 40, 41 or 42.
45. A cell according to claim 43 or 44 which is a mammalian cell or an insect cell.
46. A composition comprising a calcium channel  $\alpha_2\delta$  subunit according to any one of claims 7 to 9 and a calcium channel  $\alpha_2\delta$  subunit according to claim 10.
47. Screening assay using a calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 35.
48. Screening assay according to claim 47 which is an SPA assay, a Flashplate assay, a Nickel Flasplate assay, a Filter binding assay or a Wheat Germ Lectin flasplate assay.
49. Use of screening assay according to claim 47 or 48 to detect or measure the binding or interaction of a ligand of a calcium channel  $\alpha_2\delta$  subunit and a calcium channel  $\alpha_2\delta$  subunit.
50. Use according to claim 49 wherein the ligand is gabapentin, L-Norleucine, L-Allo-Isoleucine, L-Methionine, L-Leucine, L-Isoleucine, L-Valine, Spermine or L-Phenylalanine.
51. Kit to detect or measure the binding or interaction of a ligand of a calcium channel  $\alpha_2\delta$  subunit and a calcium channel  $\alpha_2\delta$  subunit comprising a calcium channel  $\alpha_2\delta$  subunit according to any one of claims 1 to 35.
52. Kit according to claim 51 wherein the ligand is gabapentin, L-Norleucine, L-Allo-Isoleucine, L-Methionine, L-Leucine, L-Isoleucine, L-Valine, Spermine or L-Phenylalanine.

53. Kit according to claim 51 or 52 usable in an SPA assay, a Flashplate assay, a Nickel Flasplate assay, a Filter binding assay or a Wheat Germ Lectin flasplate assay.